

## **REMARKS**

### **Amendment to Claims**

Applicants added the term "non-analgesic" to claims 8, 31 and 33. This additional term does not constitute new matter in the claims because such term was already in claims 14 and 20. Thus the Office should not consider the additional term as subject matter not previously searched.

### **Evidence Required to Establish Common Ownership**

Applicants hereby declare and affirm that U.S. Patent No. 7,030,124, filed on October 29, 2002 and published on July 31, 2003 in the name of Chang *et al.*, and assigned to Ardent Pharmaceuticals, Inc. was, at the time of filing the present invention on December 31, 2003 (U.S. Application Serial No.10/749,437), also owned by Ardent Pharmaceuticals, Inc.

### **Rejection of claims 8, 14, 20-23, 27-28, 33-34 and 38-40 under 35 U.S.C. §103(a)**

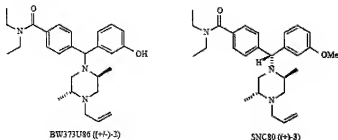
The Examiner has maintained the rejection of claims 8, 14, 20-23, 27-28, 33-34 and 38-40 under 35 U.S.C. §103(a) in view of Chang *et al.* (U.S. 7,030,124 B2, hereinafter Chang '124) in view of Schultz *et al.* (US 6,103,722, hereinafter Schultz '722). Applicants traverse such rejection.

The present application has a filing date of December 31, 2003. The Chang *et al.* reference U.S. Patent No. 7,030,124 issued on April 18, 2006 was originally published on July 31, 2003. As such the Chang *et al.* reference would be considered to meet the time requirements of a 102(e) reference and was commonly owned by Ardent Pharmaceuticals, Inc., at the time of filing of the present application. Consistent with the provisions of MPEP §706.02(l)(2), the statement hereinabove by applicants disqualifies U.S. Patent No. 7,030,124 from being used in a rejection under 35 U.S.C. §103(a) against claims of the present application. See also, MPEP §§ 706(l)(1).

Accordingly, because the Chang '124 reference has been disqualified as the primary reference, it is evident that the secondary reference is not sufficient to establish a prima facie case of obviousness.

Initially it should be noted that applicants' claimed invention relates to a method of reducing ischemic damage in cardiac tissue in a subject by using a **non-analgesic** compound for administration to a subject as a maintenance method and preferably before any negative cardiac incident.

The only compounds discussed by Schultz '722 include BW373U86 and SNC80 and having the structures below:



It is well known that these compounds, discussed by Schultz '722, exhibit strong analgesic activity and one skilled in the art of opioid chemistry is well aware of the analgesic activity of these two compounds. Each compound is a poster child for comparison with any other analgesics because of their individual high level of analgesic activity. Thus, one skilled in the art would know at the time of filing of the present invention that both the BW373U86 and SNC-80 compounds exhibited strong analgesic activity.

Notably, these compounds do not have a carboxy-substituted benzyl ring at the "4" position of the piperazine group. In fact they do not even include a ring structure connected to the N of the piperazine group. Thus, this reference does not provide any disclosure relating to the present invention.

Further, the structures of the presently claimed invention including a carboxylated benzyl ring at the lower nitrogen of the piperazine moiety does not exhibit analgesic activity as shown in Example 6 of the present invention. According to the Office, "such property or characteristic must be expected feature of said diethylmethylpiperazine within the prior art dosage range," but applicants disagree with this speculation by the Office regarding any non-analgesic activity of either SNC 80 or BW373U86. This statement by the Office is unsubstantiated and no prior art has been cited to support this speculation by the Office.

In respect of the Examiner's unsupported assertion quoted above, applicants hereby require the affidavit of the Examiner under the provisions of 37 CFR §1.104 ("Nature of examination"), which states in paragraph (c)(2) that

**"[i]n rejecting claims for want of novelty or for obviousness, the examiner must cite the best references at his or her command"**

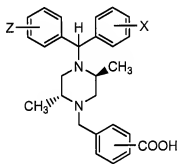
and in paragraph (d)(2) requires that

**“[w]hen a rejection in an application is based on facts within the personal knowledge of an employee of the Office, the data shall be as specific as possible, and the reference must be supported, when called for by the applicant, by the affidavit of the employee, and such affidavit shall be subject to contradiction or explanation by the affidavits of the applicant and other persons.”**  
(emphasis added)

Applicants therefore call for the examiner’s affidavit specifically supporting the Examiner’s statement that it is “such property or characteristic must be expected feature of said diarylmethylpiperazine within the prior art dosage range.”

This call for the Examiner’s affidavit is based on the fact that **applicants are unaware of any disclosure or reference that supports the Examiner’s contention of “non-analgesic” character of the compounds set forth in the Schultz reference.**

It is incumbent on the Office to provide some suggestion or teaching in the prior art that would lead one skilled in the art to proceed in the direction of applicants’ claimed invention. What is the asserted motivation put forth in the Schultz reference to synthesize **a non-analgesic** compound with the following structure:



Clearly there is none. The Courts have addressed this issue numerous times and have stated that “[t]he mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.” *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Thus, this allegedly “obvious” direction is supported only by the Office’s reinterpretation of the art in light of applicants’ disclosure.

Applicants submit that the proposed combination of Chang ‘124, which has been disqualified as competent prior art, with Shultz ‘722 does not, in any way provide derivative basis for the invention of claims 8, 14, 20-23, 27-28, 33-34 and 38-40.

**Rejection of claims 24-26, 31-32 and 35-37 under 35 U.S.C. §103(a)**

The Examiner has rejected claims 24-26, 31-32 and 35-37 under 35 U.S.C. §103(a) as being unpatentable over Chang '124 in view of Schultz '722, and further in view of Applicant's admission of the prior art (page 9, lines 5-7), which states "[O]ther cardiac therapeutic agents may include, but are not limited to nitrates, beta-adrenergic blockers, calcium channel antagonists, ACE inhibitors, non-peptide angiotensin II antagonists, IIb/IIIa antagonists and aspirin." The Examiner also cites Oeltgen (U.S. 6,645,938, herein after Oeltgen '938) to demonstrate the state of the art knowledge in using arginine hydrochloride as a cardiac therapeutic agent. Applicants respectfully traverse this rejection.

The primary reference has been disqualified and clearly the secondary and tertiary references are not sufficient to establish a *prima facie* case of obviousness. Further in light of the fact that the claimed method recited in claim 20 is novel and inventive, the addition of an additional component does not alter the patentability of the original method. Thus, the inclusion of an additional therapeutic agent in a composition does not alter the fact that the claimed compounds of the present invention are novel and inventive over the art, as is the combination with another therapeutic compound.

In summary, Applicants request that all rejections of the pending claims be withdrawn in light of the amendments and arguments made above.

**Fees Payable**

No fee is due for entry of the amendment however, if one is found due, the Commissioner is authorized to charge such fee and any addition fee found due for entry of this amendment to Deposit Account 13-4365 of Moore & Van Allen, PLLC.

**Conclusion**

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Kwon reconsider the patentability of the pending claim in light of the distinguishing remarks herein, and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Kwon is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "Marianne Fuierer", is written over a horizontal dotted line.

Marianne Fuierer

Reg. No. 39,983

Attorney for Applicants

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